

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

Claims 1-73 (canceled)

Claim 74: (currently amended) A nucleotide incorporating enzyme variant that incorporates a non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide,

wherein the nucleotide incorporating enzyme variant is encoded by a polynucleotide comprising nucleotide segments encoding all or part of two or more members of a family of parental RNA-dependent DNA polymerases,

wherein the two or more members of the family of parental RNA-dependent DNA polymerases have a pairwise identity of 77.4% or greater with respect to each other,

and

wherein the nucleotide incorporating enzyme variant is produced identified by a method comprising:

(a) providing a plurality of nucleic acid segments, which nucleic acid segments encode all or part of one the two or more parental nucleotide incorporating enzymes members of the family of parental RNA-dependent DNA polymerases;

(b) identifying at least one non-natural or rare nucleotide analogue to be incorporated by the nucleotide incorporating enzyme, which non-natural or rare nucleotide analogue is incorporated by at least one of the one two or more parental nucleotide incorporating enzymes members of the family of parental RNA-dependent DNA polymerases at an efficiency of less than about 10% the efficiency of a naturally occurring nucleotide;

(c) diversifying recombinig the plurality of nucleic acid segments, thereby producing a library of nucleic acids encoding nucleotide incorporating enzyme variants; and

(d) identifying at least one nucleotide incorporating enzyme variant that incorporates the non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide.

Claim 75 (canceled)

Claim 76 (currently amended): The nucleotide incorporating enzyme variant of claim 74, which nucleotide incorporating enzyme variant incorporates the non-natural or rare nucleotide analogue at least about 10 fold more efficiently than at least one of the one or more parental nucleotide incorporating enzymes RNA-dependent DNA polymerases.

Claims 77-78 (canceled)

Claim 79 (original): A kit comprising the nucleotide incorporating enzyme variant of claim 74, and one or more of a container, a packaging material, and a natural nucleotide or non-natural or rare nucleotide analogue.

Claim 80 (canceled)

Claim 81 (previously presented): A kit comprising the nucleotide incorporating enzyme variant of claim 76, and one or more of a container, a packaging material, and a non-natural or rare nucleotide analogue.

Claims 82-90 (canceled)

Claim 91 (currently amended): The nucleotide incorporating enzyme variant of claim 74, wherein the step of diversifying the plurality of nucleic acid segments comprises further comprising recursively recombining the plurality of nucleic acid segments.

Claim 92 (currently amended): The nucleotide incorporating enzyme variant of claim 90 74, wherein recombining the plurality of nucleic acid segments comprises assembling synthetic oligonucleotides.

Claim 93 (previously presented): The nucleotide incorporating enzyme variant of claim 92, wherein the synthetic oligonucleotides are joined using only a ligase.

Claim 94 (previously presented): The nucleotide incorporating enzyme variant of claim 91, wherein recursively recombining the plurality of nucleic acid segments comprises assembling synthetic oligonucleotides.

Claim 95 (previously presented): The nucleotide incorporating enzyme variant of claim 94, wherein the synthetic oligonucleotides are joined using only a ligase.

Claims 96-103 (canceled)

Claim 104 (new): The nucleotide incorporating enzyme variant of claim 74, wherein the RNA-dependent DNA polymerases are from a species selected from the group consisting of a *Thermus* species, a *Bacillus* species, a *Pyrococcus* species, a *Thermococcus* species, a *Thermotoga* species, and an *Anaerocellum* species.

Claim 105 (new): The nucleotide incorporating enzyme variant of claim 74, wherein at least one of the RNA-dependent DNA polymerases is from a *Thermus* species.

Claim 106 (new): The nucleotide incorporating enzyme variant of claim 105, wherein the RNA-dependent DNA polymerase is selected from the group consisting of *T. aquaticus*, *T. thermophilus*, *T. aquaticus caldophilus*, *T. filiformis*, and *T. flavis*.

Claim 107 (new): The nucleotide incorporating enzyme variant of claim 74, wherein at least one of the RNA-dependent DNA polymerases is from a species selected from the group consisting of a *Bacillus* species, a *Pyrococcus* species, a *Thermococcus* species, a *Thermotoga* species, and an *Anaerocellum* species.

Claim 108 (new): A nucleotide incorporating enzyme variant that incorporates a non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide,

wherein the nucleotide incorporating enzyme variant is encoded by a polynucleotide comprising nucleotide segments encoding all or part of more than two members of a family of parental nucleotide incorporating enzymes,

wherein the parental nucleotide incorporating enzymes have a pairwise identity of 77.4% or greater with respect to each other,

and,

wherein the nucleotide incorporating enzyme variant is identified by a method comprising:

(a) providing a plurality of nucleic acid segments, which nucleic acid segments encode all or part of the parental nucleotide incorporating enzymes from the more than two members of the family of parental nucleotide incorporating enzymes;

(b) identifying at least one non-natural or rare nucleotide analogue to be incorporated by the nucleotide incorporating enzyme, which non-natural or rare nucleotide analogue is incorporated by at least one of the parental nucleotide incorporating enzymes at an efficiency of less than about 10% the efficiency of a naturally occurring nucleotide;

(c) recombining the plurality of nucleic acid segments, thereby producing a library of nucleic acids encoding nucleotide incorporating enzyme variants; and

(d) identifying at least one nucleotide incorporating enzyme variant that incorporates the non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide.

Claim 109 (new): The nucleotide incorporating enzyme variant of claim 108, wherein the parental nucleotide incorporating enzymes are from a species selected from the group consisting of a *Thermus* species, a *Bacillus* species, a *Pyrococcus* species, a *Thermococcus* species, a *Thermotoga* species, and an *Anaerocellum* species.

Claim 110 (new): The nucleotide incorporating enzyme variant of claim 108, wherein at least one of the parental nucleotide incorporating enzymes is from a *Thermus* species.

Claim 111 (new): The nucleotide incorporating enzyme variant of claim 110, wherein the parental nucleotide incorporating enzyme is selected from the group consisting of *T. aquaticus*, *T. thermophilus*, *T. aquaticus caldophilus*, *T. filiformis*, and *T. flavis*.

Claim 112 (new): The nucleotide incorporating enzyme variant of claim 108, wherein at least one of the parental nucleotide incorporating enzymes is from a species selected from the group consisting of a *Bacillus* species, a *Pyrococcus* species, a *Thermococcus* species, a *Thermotoga* species, and an *Anaerocellum* species.

Claim 113 (new) A kit comprising the nucleotide incorporating enzyme variant of claim 108 and one or more of a container, a packaging material, and a natural nucleotide or non-natural or rare nucleotide analogue.

Claim 114: (new) A nucleotide incorporating enzyme variant that incorporates a non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide,

wherein the nucleotide incorporating enzyme variant is encoded by a polynucleotide comprising nucleotide segments encoding all or part of two or more parental nucleotide incorporating enzymes from two or more families of nucleotide incorporating enzymes,

wherein at least one parental nucleotide incorporating enzyme is an RNA-dependent DNA polymerase,

wherein the parental nucleotide incorporating enzymes from the two or more families of nucleotide incorporating enzymes have a pairwise identity of 77.4% or greater with respect to each other; and

wherein the nucleotide incorporating enzyme variant is identified by a method comprising:

(a) providing a plurality of nucleic acid segments, which nucleic acid segments encode all or part of the parental nucleotide incorporating enzymes from the two or more families of nucleotide incorporating enzymes;

- (b) identifying at least one non-natural or rare nucleotide analogue to be incorporated by the nucleotide incorporating enzyme, which non-natural or rare nucleotide analogue is incorporated by at least one of the parental nucleotide incorporating enzymes at an efficiency of less than about 10% the efficiency of a naturally occurring nucleotide;
- (c) recombining the plurality of nucleic acid segments, thereby producing a library of nucleic acids encoding nucleotide incorporating enzyme variants; and
- (d) identifying at least one nucleotide incorporating enzyme variant that incorporates the non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide.

Claim 115 (new): The nucleotide incorporating enzyme variant of claim 114, wherein at least one parental nucleotide incorporating enzyme is from a family of nucleotide incorporating enzymes selected from the group consisting of terminal transferases, ligases, and telomerases.

Claim 116 (new): A kit comprising the nucleotide incorporating enzyme variant of claim 114 and one or more of a container, a packaging material, and a natural nucleotide or non-natural or rare nucleotide analogue.